UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/635,433	08/10/2000	Mark C. Noe	PC10491A	6255

7590 10/09/2003

Paul H Ginsburg
Pfizer Inc
235 East 42nd Street 20th Floor
New York, NY 10017-5755

EXAMINER	
MCKENZIE, THOMAS C	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 10/09/2003

20

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/635,433	NOE ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to amendments filed on 9/15/03. Applicant has amended claim 16. There are five claims pending and five under consideration. Claims 16-20 are use claims. This is the fourth action on the merits. The application concerns some uses of aggrecanase inhibitors having both a carboxylic acid hydroxamide functional group and a phenol benzyl ether.

Response to Amendment

2. Applicants' new partial structure overcomes the anticipation rejections made in the previous action. None of the references previously applied teach compounds with the newly required phenol benzyl ether.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. What chemical structure is implied by the wavy line in the upper right hand corner of the formula of claim 16? Dangling valences are not permitted, *Ex parte Diamond* 123 USPQ 167. An essential portion of the molecule whose use is claimed is not defined, *Ex parte Pedlow* 90 USPQ 395.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-20 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as reasonably to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. What are the chemical structures of the aggrecanase inhibitors whose use Applicants claim? Beyond molecular weight, the presence of a single functional group, and a desired pharmacological activity, Applicants do not demonstrate that they understand the structures of these molecules. According to the MPEP § "[a]n applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, **structures** [emphasis added], figures, diagrams, and **formulas** [emphasis added], that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or **structural chemical formulas** [emphasis added], that show that the invention was

complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S. Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). "Compliance with the written description requirement is essentially a fact-based inquiry that will necessarily vary depending on the nature of the invention claimed. '" *Enzo Biochem*, 296 F.3d at 1324, 63 USPQ2d at 1613." Applicants limited structural information is not sufficient to distinguish the compounds whose use they claim.

5. Claims 16-20 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making the compounds of Formula I on page 5, does not reasonably provide enablement for making all the carboxylic acid hydroxamide compounds with the desired aggrecanase activity they intend to use. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Since Applicants do not specify the structures of the compounds they intend to use, how can the skilled process chemist be expected to

make these compounds? Directions to the pharmacologist for how to seek such compounds hardly constitute directions to the chemist of how to make them.

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) Making any particular substrate would require ascertaining its chemical structure, devising a synthesis of the compound, and successfully preparing the substance in the laboratory. Since there is no direction concerning the first step, no degree of experimentation would be sufficient to perform this task. b) The direction concerning compound synthesis is found in the passage spanning line 14, page 21 through line 15, page 50. This passage concerns only synthesis of compounds of formula I. There is no direction concerning the synthesis of any other compounds meeting Applicants claim limitations. c) There are working examples of synthesis of compound of formula (I) in the passage spanning line 1, page 65 to line 32, page 82. There are no working examples of synthesis of compounds not fitting formula I.

d) The nature of the invention requires both chemical synthesis, which involves chemical reactions, and therapeutic activity. e) The state of the art is summarized in pages 1-4 of the specification. f) The artisan using Applicants invention to prepare the claimed compounds would be a process chemist or pilot plant operator with a BS degree in chemistry and several years of experience. g) Chemical reactions are well-known to be unpredictable, *In re Marzocchi*, 169 USPQ 367, *In re Fisher*, 166 USPQ 18. h) The breadth of the claims includes the six diseases mentioned in claim 16 as well as the presently unknown list of compounds embraced by claim 16.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

The two first paragraph rejections will be considered together. Applicants make two arguments. Firstly, that the additional layer of added structural information, when coupled by the functional limitations, is sufficient to both

describe and allow the process chemist to prepare the compounds whose use they desire. Secondly, that only routine screening will be required to test for the aggrecanase activity specified. Neither argument is persuasive.

As to the added structural detail, according to the MPEP § 2163, Section A, which says in part, "However, as discussed in paragraph I., supra, the issue of a lack of adequate written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant had possession of the claimed invention. The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art" and "The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function." "A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process."

The radical connecting the benzyl ether and the carboxamide functional groups is an essential feature. The question then, is, what structural limitations would the skilled process chemist infer from the phrase "the carboxylic acid hydroxamide derivative exhibits an aggrecanase IC_{50} of less than about 20 nM". Applicants do not assert and it is not art-recognized that such a phrase allows the missing portion of the molecule to be immediately envisaged.

As to the routine screening for aggrecanase activity, firstly, the enablement rejection concerns the synthesis of the compounds to be used. Without the compounds in hand, Applicants cannot practice their invention. Screening the compounds, routine or not, neither makes the compounds nor does it teach how to make them. In fact, screening compounds has nothing to do with making the compounds. Secondly, Applicants are instructed to look at page 31 of Judge Larimer's opinion in University of Rochester v G.D. Searle from the District Court from the Western District of New York. This can be found at http://www.nywd.uscourts.gov/decision/20030305_00cv6161_larimer.pdf. The screening of 600 existing compounds over an eight-month period was given as an example of undue experimentation. Can one imagine what Judge Larimer's would have thought of the amount of experimentation required to make those 600 compounds? Especially when the only method of finding them is trial and error.

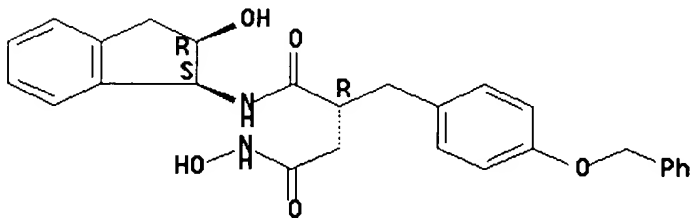
Do Applicants intend to apply trial and error methods to the synthesis of all the compounds whose use they claim?

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

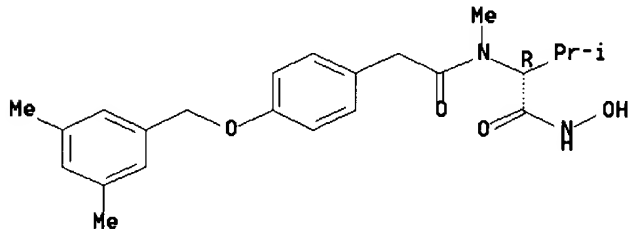
Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated or, in the alternative, under 35 U.S.C. 103(a) as obvious by Yau ('664). There is one N-hydroxyl carboxyl amide compound that also contains a benzyl ether of a phenol taught in this reference. That compound is shown below. It fits the partial formula of claim 16 with $R^5 = R^6$ = hydrogen. It has registry number 220681-99-2 and may be found in column 66, line 16 of the reference. It is compound 10. The ability of this compound to inhibit the enzyme aggrecanase and to treat arthritis is taught in lines 25-33, column 4. The reference is silent as to the IC_{50} of aggrecanase enzyme



inhibition exhibited by this compound. However, "recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not cause a claim drawn to those things to distinguish over the prior art. Additionally, where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on. [58 CCPA at 1031, 439 F.2d at 212-13, 169 USPQ at 229.] This burden was involved in *In re Ludtke*, 58 CCPA 1159, 441 F.2d 660, 169 USPQ 563 (1971), and is applicable to product and process claims reasonably considered as possessing the allegedly inherent characteristics." *In re Swinehart*, 58 CCPA 1027, 439 F.2d 210, 169 USPQ 226 (1971), *In re Best, Bolton, and Shaw,* 195 USPQ 430 (CCPA 1977).

7. Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated or, in the alternative, under 35 U.S.C. 103(a) as obvious by Duan ('665). There are eight N-hydroxyl carboxyl amide compound that also contains a benzyl ether of a phenol taught in this reference. One such compound is shown below. It fits the partial formula of claim 16 with $R^5 = R^6 =$ *m*-methyl. It has registry number 301162-25-4 and may be found in column 47, line 20. It is compound 23. The other

anticipatory compounds are found throughout Table 1 of the reference. The ability of these compounds to inhibit aggrecanase in taught in lines 40-43, column 101. The ability to treat inflammatory diseases is taught in lines 3-18, column 102. The

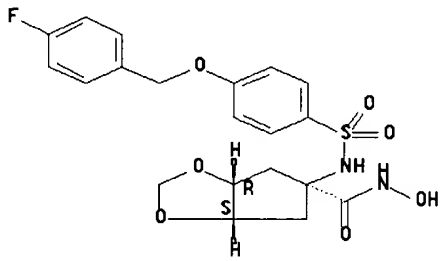


reference is silent as to the IC_{50} of aggrecanase enzyme inhibition exhibited by this compound. However, "recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not cause a claim drawn to those things to distinguish over the prior art. Additionally, where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on. [58 CCPA at 1031, 439 F.2d at 212-13, 169 USPQ at 229.] This burden was involved in *In re Ludtke*, 58 CCPA 1159, 441 F.2d 660, 169 USPQ 563 (1971), and is applicable to product and process claims reasonably considered as possessing the allegedly inherent characteristics." *In re Swinehart*,

58 CCPA 1027, 439 F.2d 210, 169 USPQ 226 (1971), *In re Best, Bolton, and Shaw,* 195 USPQ 430 (CCPA 1977).

8. Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated by McClure ('870). The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

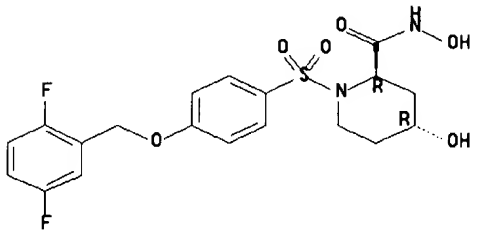
There are three N-hydroxyl carboxyl amide compounds that also contain a benzyl ether of a phenol taught in this reference. One such compound is shown below. It fits the partial formula of claim 16 with R^5 = *p*-fluoro. It has registry number 298195-25-2 and may be found in the passage spanning line 46, column 35 to line 8, column 36. It is Example 7. The other anticipatory compounds are Examples 6 and Example 8. Inhibition of aggracanase is taught the passage spanning line 66, column 1 to line 2, column 2. Treatment of arthritis with these compounds is found in claim 30 of the reference. The reference is silent as to the



IC_{50} of aggrecanase enzyme inhibition exhibited by this compound. However, "recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not cause a claim drawn to those things to distinguish over the prior art. Additionally, where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on. [58 CCPA at 1031, 439 F.2d at 212-13, 169 USPQ at 229.] This burden was involved in *In re Ludtke*, 58 CCPA 1159, 441 F.2d 660, 169 USPQ 563 (1971), and is applicable to product and process claims reasonably considered as possessing the allegedly inherent characteristics." *In re Swinehart*, 58 CCPA 1027, 439 F.2d 210, 169 USPQ 226 (1971), *In re Best, Bolton, and Shaw,* 195 USPQ 430 (CCPA 1977).

9. Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated by McClure ('397). The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

There are sixty-six N-hydroxyl carboxyl amide compounds that also contain a benzyl ether of a phenol taught in this reference. One such compound is shown below. It fits the partial formula of claim 16 with R^5 = *o*-fluoro and R^6 = *m*-fluoro. It has registry number 258860-57-0 and may be found in columns 71 and 72 of the reference. It is Example 41. The other anticipatory compounds may be found throughout Tables I-IV. Inhibition of aggracanase is taught the passage spanning line 66, column 1 to line 2, column 2. Treatment of arthritis with these compounds is found in claim 68 of the reference. The reference is silent as to the IC_{50} of



aggrecanase enzyme inhibition exhibited by this compound. However, "recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not cause a claim drawn to those things to distinguish over the prior art. Additionally, where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on. [58 CCPA at 1031, 439 F.2d at 212-13, 169 USPQ at 229.] This burden was involved in *In re Ludtke*, 58 CCPA 1159, 441 F.2d 660, 169 USPQ 563 (1971), and is applicable to product and process claims reasonably considered as possessing the allegedly inherent characteristics." *In re Swinehart*, 58 CCPA 1027, 439 F.2d 210, 169 USPQ 226 (1971), *In re Best, Bolton, and Shaw,* 195 USPQ 430 (CCPA 1977).

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to

prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 30 of U.S. Patent No. 6,214,870 Although the conflicting claims are not identical, they are not patentably distinct from each other because of the reasons discussed above.

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude"

granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 68 of U.S. Patent No. 6,329,397. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the reasons discussed above.

Conclusion

12. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX.

The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, you can reach the Examiner's supervisor, Mukund Shah at (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

Thomas C. McKenzie, Ph.D.
Patent Examiner
Art Unit 1624

TCMcK